# Cardiac Magnetic Resonance Follow-Up of Children After Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 With Initial Cardiac Involvement

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**Background:** Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) is an inflammatory disease occurring in a small minority of children a few weeks after acute infection. Cardiac manifestations are common, but little is known about the potentially persistent heart changes after PIMS-TS.
**Purpose:** To analyze the frequency and type of myocardial complications of PIMS-TS with initial cardiac involvement assessed with cardiac magnetic resonance imaging (MRI), including parametric imaging, performed 3 months after hospitalization.
**Study Type:** Retrospective.
**Population:** Nineteen consecutive children (median age 10 years, interquartile range (IQR) 10–15 years, 74% male).
**Field Strength/Sequence:** Balanced steady state free precession (bSSFP, cine imaging), modified Look-Locker (T1 mapping), T2-prepared bSSFP (T2-mapping), dark-blood T2-weighted turbo spin echo with fat suppression and phase sensitive inversion recovery (late gadolinium enhancement (LGE)) sequences at 1.5 T.
**Assessment:** Patients were scanned after a median of 99 days (IQR 89–104 days) from the diagnosis. MR data were reviewed by three independent observers, with 13, 2, and 5 years' experience in cardiac MRI. Pre- and post-contrast T1, T2, extra-cellular volume, and T2 signal intensity (T2 SI) ratio were calculated. Diagnosis of acute myocarditis was based on modified Lake Louise criteria. Cardiac MRI parameters were compared, where possible, to previously published pediatric normal values.
**Statistical Tests:** Interclass correlation coefficient and Bland–Altman repeatability analysis. A *P*-value <0.05 was considered statistically significant.
**Results:** Despite cardiac involvement including decreased left ventricular ejection fraction (LVEF) (median LVEF = 47%, IQR 43%–53%) and increased troponin I (median 101 ng/mL, IQR 50–661 ng/mL) during hospitalization, there were no persistent cardiac changes observed in cardiac MR at follow-up. All patients had normal size and function of the left ventricle and normal precontrast T1 and T2 relaxation times. There were no signs of LGE. Persistent, mild pericardial effusion (8–9 mm) was found in three (16%) patients.
**Data Conclusion:** There were no persistent changes on cardiac MRI in a group of children approximately 3 months post hospitalization due to PIMS-TS with cardiac involvement. This supports the hypothesis that cardiac involvement during PIMS-TS is a form of transient inflammatory response rather than direct and potentially persistent injury from the virus.
**Level of Evidence:** 4
**Technical Efficacy:** Stage 3

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Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) or multisystem inflammatory syndrome in children (MIS-C) is an inflammatory disease occurring in a minority of children a few weeks after acute infection with SARS-CoV-2.[1,2] It has been defined by the World Health Organization (WHO) as

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the presence of 1) fever persisting for at least 3 days; 2) elevated inflammatory markers (eg, erythrocyte sedimentation rate, C-reactive protein (CRP), or procalcitonin); 3) multisystem involvement (rash, bilateral nonpurulent conjunctivitis, mucocutaneous inflammation, hypotension or shock, cardiac dysfunction, coagulopathy, and acute gastrointestinal symptoms); 4) evidence of SARS-Cov-2 infection by polymerase chain reaction (PCR), serology, antigen, or an exposure to an individual with Covid-19; and 5) no obvious other microbial cause of inflammation.[3]

PIMS-TS is most likely caused by deregulated inflammatory response to the virus rather than by direct injury from the SARS-CoV-2.[1,2] Cardiac manifestations are common including ventricular dysfunction, arrhythmias, conduction abnormalities, and coronary artery dilation.[1,2] In a study presenting the clinical course in children with PIMS-TS, 29 (50%) out of 58 patients developed shock.[4] In children with cardiac involvement, left ventricular dysfunction on echocardiography and troponin elevation were found in 62% and 66% of cases, respectively, with N-terminal pro-brain natriuretic peptide (NT-proBNP) increased in all cases.[4] In a systematic review of PIMS-TS, decreased left ventricular ejection fraction (LVEF) was found in 45.1% of cases, with severe decrease (<30%) in 5%, while pericardial effusion was reported in 22% of cases.[2]

The majority of patients recover within days to weeks with supportive therapy and treatment with immune-modulatory medications leading to low mortality.[1] However, long-term consequences, particularly cardiovascular are not precisely defined.[1,2,5] A few small case reports with cardiac magnetic resonance imaging (MRI) performed 1–4 weeks since hospital admission or initial symptoms have reported conflicting results.[6–8] One small case series demonstrated diffuse myocardial edema with no evidence of replacement fibrosis or focal necrosis.[6] A study on 20 children found myocardial edema in 50% of cases with three cases of speckling late gadolinium enhancement (LGE) and one subendocardial scar typical of ischemic injury.[7] Another small case report did not disclose any signs of acute myocarditis or fibrosis.[8]

The discrepancies between reported studies may come from the fact that most of them did not use parametric imaging (T1-mapping, T2-mapping), which has been shown to increase diagnostic accuracy for detection of myocardial injury.[9] Currently, to establish the true rate of potential cardiac complications post PIMS-TS, most centers recommend follow-up cardiac MRI to be performed 3 months after the presentation, but these data are currently lacking.[5–8,10] Follow-up data are also needed to indirectly analyze the etiology of cardiac involvement in PIMS-TS as lack of persistent cardiac changes would support inflammatory reaction to the virus as etiology of PIMS-TS rather than direct myocardial injury by the SARS-CoV-2. With typical "pre-SARS-CoV-2 era" myocarditis with direct myocardial injury by the virus, persistent fibrosis, or even signs of persistent acute myocarditis have been demonstrated in a subset of children even at 3–9 months follow-up.[11–14]

Thus the aim of this single-center study was to analyze the frequency and type of myocardial complications of PIMS-TS with initial cardiac involvement assessed with cardiac MRI, including parametric imaging, performed 3 months after hospitalization.

## Materials and Methods

### Ethical Considerations

This study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Ethics Committee of Medical University of Warsaw (no. KB/13/2017).

### Study Group

This retrospective analysis included 19 children (Caucasian, median age 10 years (interquartile range (IQR) 10–15 years), 74% male) hospitalized for PIMS-TS in Children's Clinical Hospital in Warsaw between November 2020 and January 2021 with initial documentation of cardiac involvement defined as decreased left ventricular ejection fraction (<55%) on echocardiography during hospitalization and/or elevated concentration of troponin I (TnI) (<19 ng/mL as per local laboratory reference values).

Detailed characteristics of symptoms, SARS-CoV-2 PCR and/or serology results, laboratory markers, left ventricular systolic function during hospitalization, immune-modulatory treatment, and time of hospital stay are presented in Table 1.

Apart from fever, which was present in all patients on admission, dominating symptoms included those of the gastrointestinal system (abdominal pain, vomiting, diarrhea) present in 13 patients (68%), followed by cough in four (21%) patients, headache and/or lymphadenopathy present in three (16%) patients, rash and/or sore throat in two (11%) patients, and single cases (5%) of dyspnea and chest pain or swollen hands and feet. Two (11%) patients were admitted in shock. All patients had positive IgG test for SARS-CoV-2, while positive IgM and/or PCR tests were found in 10 (53%) children.

CRP and D-dimers were elevated in all patients with median values of 20 mg/L (IQR 12–32 mg/L, reference values <1 mg/L) and 3203 ng/mL (IQR 1444–4463 ng/mL, reference values <550 ng/mL), respectively. TnI was elevated in 16 (84%) patients with median values of 101 ng/mL (IQR 50–661 ng/mL, reference values <19 ng/mL), while NT-proBNP was increased in 18 (95%) patients with median values of 5129 pg/mL (IQR 1975–13179 pg/mL, reference values <125 pg/mL).

Decreased systolic function of the left ventricle (LV) on echocardiography was found in 18 (95%) children with median values of 47% (IQR 43%–53%). Patient 6 had normal LVEF, but elevated TnI therefore fulfilling the definition of cardiac involvement during PIMS-TS. Two children admitted in shock had the lowest LVEF—30% and 34%. Mild to moderate pericardial effusion was present in 4 patients ranging from 4 to 13 mm.

All patients responded well to immune-modulatory treatment consisting of intravenous immunoglobulin in all cases and steroids in more severe cases (11 patients, 63%). Median time of hospitalization was 11 days (IQR 7–14.5 days). All children were discharged in

**TABLE 1. Baseline and Clinical Data of the Studied Patients**

| ID | Age (Years) | Sex | Symptoms | Positive PCR or Serology for SARS-CoV-2 | CRP_Max (mg/L)[a] | D-Dimers (ng/mL)[a] | TnI_Max (ng/L)[a] | BNP_Max (pg/mL)[a] | Lowest LVEF on TTE (%) | Immune-Modulatory Treatment | Time of Hospitalization (Days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 15 | M | Fever, shock | IgG | 32 | 4545 | 3322 | 57,508 | 30 | IVIG, S | 24 |
| 2 | 10 | M | Fever, swollen hands and feet, vomiting, myalgia | IgG, IgM | 82 | 4381 | 0 | 1854 | 54 | IVIG, S | 11 |
| 3 | 12 | M | Fever, abdominal pain, diarrhea | IgG | 12 | 1435 | 7 | 619 | 44 | IVIG, S | 14 |
| 4 | 9 | M | Fever, abdominal pain | IgG, IgM | 11 | 3059 | 95 | 21,603 | 47 | IVIG, S | 7 |
| 5 | 15 | M | Fever, abdominal pain, diarrhea | IgG | 15 | 1630 | 1390 | 60 | 50 | IVIG | 10 |
| 6 | 17 | F | Fever, rash | IgG, IgM | 19 | 1155 | 36 | 152 | 65 | IVIG | 5 |
| 7 | 12 | M | Fever, abdominal pain, vomiting, diarrhea | IgG | 17 | 2 843 | 12784 | 1975 | 43 | IVIG, S | 14 |
| 8 | 17 | F | Fever, vomiting, lymphadenopathy | PCR, IgG, IgM | 31 | 13800 | 14 | 5925 | 55 | IVIG | 7 |
| 9 | 9 | M | Fever, vomiting | IgG, IgM | 35 | 1843 | 237 | 43,795 | 35 | IVIG, S | 15 |
| 10 | 12 | M | Fever, diarrhea | IgG, IgM | 23 | 4606 | 50 | 2722 | 41 | IVIG | 6 |
| 11 | 14 | M | Fever, headache, cough | IgG | 31 | 1452 | 101 | 5328 | 48 | IVIG, S | 8 |
| 12 | 14 | F | Fever, abdominal pain, vomiting, headache | IgG, IgM | 170 | 4256 | 118 | 5731 | 43 | IVIG, S | 13 |
| 13 | 10 | F | Fever, abdominal pain, cough | IgG, IgM | 3 | 5844 | 92 | 15,000 | 45 | IVIG, S | 17 |
| 14 | 8 | F | Fever, shock | IgG | 1.5 | 2832 | 91 | 3871 | 34 | IVIG, S | 26 |
| 15 | 15 | M | Fever, sore throat | IgG | 14 | 3936 | 277 | 13,179 | 47 | IVIG | 5 |

**TABLE 1. Continued**

| ID | Age (Years) | Sex | Symptoms | Positive PCR or Serology for SARS-CoV-2 | CRP_Max (mg/L)[a] | D-Dimers (ng/mL)[a] | TnI_Max (ng/L)[a] | BNP_Max (pg/mL)[a] | Lowest LVEF on TTE (%) | Immune-Modulatory Treatment | Time of Hospitalization (Days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 9 | M | Fever, vomiting, diarrhea, headache, lymphadenopathy, cough | IgG, IgM | 20 | 7779 | 661 | 13,128 | 45 | IVIG, S | 9 |
| 17 | 11 | M | Fever, abdominal pain, lymphadenopathy, rash | IgG | 12 | 4242 | 71 | 4345 | 53 | IVIG | 7 |
| 18 | 13 | M | Fever, abdominal pain | IgG | 39 | 3348 | 588 | 1981 | 57 | IVIG | 11 |
| 19 | 14 | M | Fever, sore throat, cough, chest pain, dyspnea | PCR, IgG | 30 | 733 | 4356 | 5129 | 49 | IVIG, S | 14 |

CRP = C-reactive protein; IVIG = intravenous immunoglobulin; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-brain natriuretic peptide; PCR = polymerase chain reaction test; TnI = troponin I; S = steroids; TTE = transthoracic echocardiography.
[a]Normal ranges: BNP <125 pg/mL; CRP <1 mg/L; D-dimer <550 ng/mL; TnI < 19 ng/L; LVEF <55%.

good clinical condition, free of symptoms, with normalized laboratory markers and normal LVEF on transthoracic echocardiography. Cardiac MRI was not performed during the hospitalization. After recovery, all patients were scheduled for a follow-up cardiac MRI at 3 months post discharge. PIMS-TS was diagnosed according to WHO criteria.[3]

### MR Protocol and Analysis

The study was performed with the use of a Siemens Sola 1.5 Tesla scanner (Siemens, Erlangen, Germany). The protocol included initial scout images, followed by cine balanced steady-state free precession (bSSFP) breath-hold sequences in two-, three-, and four-chamber views. Short axis was identified using the two- and four-chamber-images and a stack of images acquired which included the ventricles from the mitral and tricuspid valvular plane to the apex.

Precontrast T1-mapping with a modified Look-Locker sequence and T2-mapping with a T2-prepared SSFP sequence were performed immediately after acquisition of the bSSFP cine images and processed using MyoMaps software (Siemens, Erlangen, Germany). For that purpose, three short-axis slices (one basal, one mid-ventricular and one apical) and two-, three-, and four-chamber views were obtained. Subsequently an acquisition of dark-blood T2-weighted (T2W) turbo spin echo images with fat suppression in the same orientations was performed.

Following these acquisitions, 0.1 mmol/kg of a gadolinium contrast agent (gadobutrol—Gadovist, Bayer Shering Pharma AG, Berlin, Germany) was administered and flushed with 15 mL of isotonic saline. LGE images in three long axis and a stack of short-axis imaging planes were obtained with a breath-hold phase-sensitive inversion recovery sequence 5–15 minutes after the contrast injection. The inversion time was adjusted to null normal myocardium (typically between 250 and 350 msec as assessed by means of a TI-scout acquisition). This was followed by a postcontrast T1-mapping acquisition 15 minutes after the contrast injection in the same orientations as the precontrast T1-mapping.

Images were analyzed with the use of dedicated software (Syngovia, Siemens, Erlangen, Germany). All studies were assessed independently by three physicians—one cardiologist and two radiologists, each with expertise in cardiac MR (Ł.A.M.—13 years of experience, M.B. and M.B-F.—2 and 5 years of experience, respectively). End-diastolic and end-systolic endocardial and epicardial contours were drawn semi-automatically for the LV in the short-axis stack of bSSFP cine acquisitions. Delineated contours were used for the quantification of end-diastolic (LVEDVI) and end-systolic volume (LVESVI), stroke volumes (LVSVI), and ejection fraction (LVEF) indexed to body surface area. We used previously published pediatric normal values of left and right ventricular volumes, systolic function, and mass as a reference.[15]

Precontrast T1 and T2 maps as well as T2W images were initially assessed visually for the presence of hyperintense areas. Precontrast T1 and T2 relaxation times, T2 signal intensity (T2 SI) ratios, and postcontrast T1 relaxation times were calculated from a 0.7 $cm^2$ region of interest (ROI) placed in the mid-ventricular short-axis slice in the mid-section of the interventricular septum avoiding the right ventricle/LV insertion points and the hyperintense area, if visible. Caution was taken not to include LGE areas in the measurements and not to include blood pool in the ROI. For blood pool pre- and postcontrast T1 calculation, a ROI of the same size was placed at the same level in the ventricular cavity, but separate from the papillary muscles or trabeculations. For T2 SI ratio, a ROI in the skeletal muscles of the chest of the same size was used. Extracellular volume (ECV) was calculated using the previously validated equation, with hematocrit being assessed from a blood sample.[16]

The presence and location of LGE was assessed visually. Abnormal native T1 and T2 values were defined as greater than 1086 msec and greater than 52 msec, respectively, based on previously derived sequence and scanner-specific cutoffs of 2 SDs above the respective means in a healthy pediatric population.[17,18] Increase of myocardial T2 SI ratio was defined as a signal intensity ratio of the LV myocardium to skeletal muscle ≥2.0.[20] Acute myocarditis was defined according to the updated Lake Louise criteria using a T2-based criterion in combination with a T1-based criterion.[19] We have reported ECV values, but were unable to find reference values for the pediatric population as all reported values were performed with the use of a different type and amount of contrast agent and some did not report timing between contrast administration and postcontrast T1-mapping acquisition.[17,18]

### Statistical Analysis

All results for categorical variables were presented as a number and a percentage. Continuous variables were expressed as median and IQR. Inter- and intra-reader variability were assessed in 13 randomly chosen children using interclass correlation coefficient (ICC) and Bland–Altman repeatability analysis between one and two readers (cardiologist and one of the radiologists), respectively. Interobserver variability was determined for the most experienced reader (Ł.A.M, 13 years) and one of the radiologists (M.B-F., 5 years). Intraobserver variability was assessed for one of the radiologists (M.B., 2 years). The interval between analyses was 1 month. All tests were two-sided with the significance level of $P < 0.05$. Statistical analyses were performed with MedCalc statistical software 10.0.2.0 (Ostend, Belgium).

## Results

### Cardiac MRI

Patients were scanned after a median of 99 days (IQR 89–104 days) from the diagnosis. Cardiac MRI volumetric, functional, and tissue characteristics are presented in Table 2.

All patients had normal left ventricular size (median LVEDVI 70 mL/$m^2$, IQR 65–78 mL/$m^2$), and function (median LVEF 64%, IQR 61%–68%). Precontrast T1 and T2 times were within normal limits in all patients. T2-mapping was incidentally not performed in patient 2; however, no other parameter was altered in that case (as described below). T2 SI was slightly elevated only in patient 18, with no other changes found on cardiac MRI and only mild-to-moderate signs of initial cardiac involvement (LVEF = 57%, TnI 588 ng/mL). There was no LGE observed in any patient and median ECV in the whole group was 28.4% (IQR 26.1%–30.1%). Patient 13 did not have hematocrit measured and therefore ECV could not be calculated in this case. Altogether, no patient had signs of ongoing acute myocarditis or persistent myocardial scars.

**TABLE 2. Cardiac MRI Volumetric, Functional, and Tissue Characteristics Pattern**

| ID | LVEDVI (mL/m$^2$) | LVESVI (mL/m$^2$) | LVSV (mL/m$^2$) | LVEF (%) | LVMI (g/m$^2$) | T1 pre (msec) | T1 post (msec) | T2 (msec) | T2 SI | Pericardial effusion (mm) | LGE | ECV (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 66 | 24 | 42 | 64 | 59 | 1010 | 565 | 41 | 1.43 | – | – | 25.1 |
| 2 | 69 | 21 | 48 | 70 | 52 | 1053 | 591 | | 1.31 | – | – | 29.0 |
| 3 | 95 | 38 | 57 | 60 | 69 | 999 | 643 | 45 | 1.76 | 8 | – | 28.2 |
| 4 | 75 | 19 | 56 | 74 | 52 | 1024 | 633 | 45 | 1.44 | – | – | 31.0 |
| 5 | 65 | 25 | 40 | 61 | 52 | 1003 | 596 | 44 | 1.46 | – | – | 24.4 |
| 6 | 63 | 20 | 42 | 67 | 56 | 1062 | 630 | 47 | 1.60 | 9 | – | 32.1 |
| 7 | 76 | 28 | 48 | 63 | 49 | 1040 | 651 | 43 | 1.87 | – | – | 27.6 |
| 8 | 72 | 30 | 42 | 59 | 54 | 990 | 529 | 44 | 1.76 | – | – | 26.1 |
| 9 | 63 | 23 | 40 | 64 | 61 | 1033 | 608 | 44 | 1.37 | – | – | 29.0 |
| 10 | 88 | 27 | 61 | 69 | 64 | 1035 | 610 | 47 | 1.69 | – | – | 26.1 |
| 11 | 83 | 33 | 50 | 60 | 48 | 968 | 612 | 43 | 1.93 | – | – | 26.5 |
| 12 | 90 | 36 | 54 | 60 | 62 | 1044 | 564 | 43 | 1.89 | – | – | 29.2 |
| 13 | 69 | 22 | 47 | 68 | 43 | 1037 | | 42 | 1.50 | 7 | – | |
| 14 | 70 | 21 | 49 | 70 | 37 | 1014 | 642 | 51 | 1.70 | – | – | 30.6 |
| 15 | 78 | 29 | 50 | 64 | 55 | 1032 | 614 | 42 | 1.29 | – | – | 30.1 |
| 16 | 60 | 21 | 39 | 65 | 50 | 1053 | 577 | 45 | 1.41 | – | – | 28.5 |
| 17 | 71 | 24 | 46 | 66 | 52 | 1055 | 578 | 45 | 1.53 | – | – | 30.8 |
| 18 | 67 | 22 | 45 | 67 | 46 | 1031 | 595 | 46 | 2.24 | – | – | 27.8 |
| 19 | 64 | 25 | 41 | 61 | 56 | 985 | 533 | 43 | 1.20 | – | – | 23.8 |

ECV = extracellular volume; LGE = late gadolinium enhancement; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVI = left-ventricular end-systolic volume index; LVMI = left ventricular mass index; LVSVI = left ventricular stroke volume index; T1 pre = T1 relaxation time before contrast administration; T1 post = T1 relaxation time after contrast administration; T2 = T2 relaxation time; T2 SI ratio = ratio of signal intensity between myocardium and skeletal muscle on T2W image.

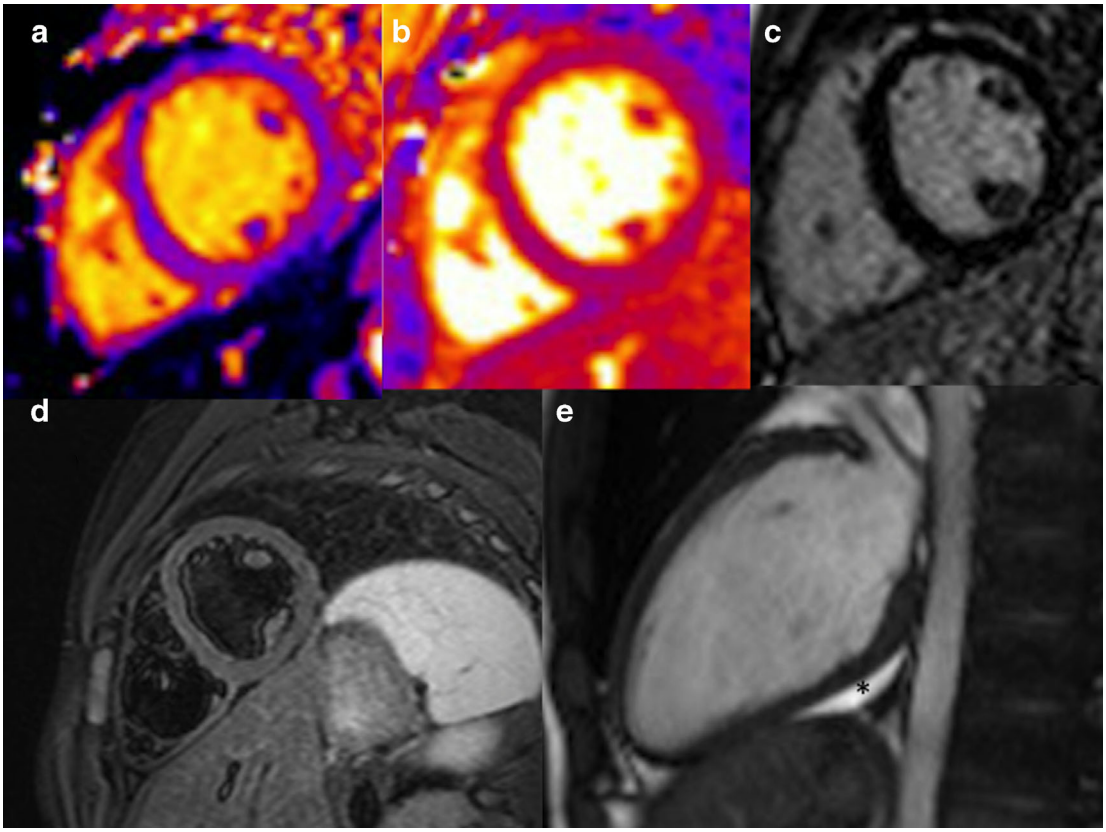


**FIGURE 1: Examples of most typical cardiac MRI findings in the studied group (a—normal precontrast T1 map, b—normal T2 map, c—lack of LGE, d—normal T2W image; all in short-axis mid-ventricular views) and less typical small amount of pericardial effusion (e—two-chamber view, pericardial effusion marked with asterisk). See Table 2 for abbreviations.**

A small amount of pericardial effusion (7–9 mm) was still present in three (16%) patients, who also had pericardial effusion on echocardiography during hospitalization, and had completely resolved in one other child. There was no statistical relation between the presence of pericardial effusion and baseline characteristics or clinical course of PIMS-TS.

Examples of typical cardiac MRI images in the studied group and less typical persistent pericardial effusion are presented in Figure 1.

### *Intra- and Inter-Reader Variability*

There was low intra- and inter-reader variability. The ICC and Bland–Altman bias were, respectively, 0.99 and 1.8 ± 4.0 msec for preconstrast T1, 0.87 and 0.4 ± 0.6 msec for T2, and 0.93 and 0.05 ± 0.03 for T2 SI ratio for intra-reader variability. For inter-reader variability the ICC and Bland–Altman bias were, respectively, 0.97 and 2.2 ± 6.1 msec for T1, 0.89 and 0.2 ± 0.8 msec for T2, and 0.92 and 0.01 ± 0.05 for T2 SI ratio.

## Discussion

We have demonstrated that there were no clinically significant persistent cardiac changes on cardiac MRI at mid-term follow-up post PIMS-TS with cardiac involvement in one of the largest groups of patients studied with this technique. Our observations are similar to recently reported results of Webster et al, where patients 2 months after COVID or MIS-C diagnosis revealed no abnormalities on cardiac MRI and cardiac biomarkers.[21] Previous studies in children with PIMS-TS performed with cardiac MRI in the first month from the diagnosis have shown mainly myocardial edema[6] without fibrosis suggesting only transient inflammatory reaction rather than direct and potentially persistent myocardial injury from the SARS-CoV-2. However, there have also been reports of fibrosis [7,10] and even subendocardial (ischemic type) scars[7] leaving the debate on the mechanism of cardiac injury during PIMS-TS still open.

Our results are reassuring and support the hypothesis of lack of direct cardiac tropism of the virus. In analyses of myocarditis resolution in children after infection with typical cardio tropic viruses in "pre-SARS-CoV-2 era," persistent changes on cardiac MRI were commonly shown at 6–9 months follow-up. In the study by Banka et al repeated MRI was done after median 6 months in 52 children initially diagnosed with myocarditis and demonstrated persistent LGE in 39 patients and new LGE in four previously LGE-negative patients (together—85%) with persistently negative or resolved LGE in only 15% of children.[12] Signs of myocardial edema on T2W images were still present in six (17%) out of 35 patients, in whom T2W imaging was performed at both presentation and follow-up. In another study on

18 adolescents, cardiac MRI disclosed ongoing active inflammation in five (28%) patients, healed myocarditis with persistent scars in eight (44%) patients, and complete resolution of initially observed changes only in five (28%) patients after a median follow-up of 7 months despite complete recovery of symptoms, normalization of cardiac biomarkers, and LVEF.[14] These results are in contrast with the findings of the current analysis which demonstrated only one doubtful case of persistent myocardial edema on T2W imaging (5%) and no LGE at a much shorter follow-up period.

Our findings are further supported by comprehensive assessment, including T1- and T2-mapping, which were not used in the two previously reported studies on cardiac MRI post myocarditis in children.[12,14] It has been shown that parametric imaging is able to detect more subtle myocardial injury or ongoing myocardial inflammation compared to traditional cardiac MRI implementing only T2W and LGE techniques.[9] In a study by Luetkens et al on 24 adults initially diagnosed with myocarditis on cardiac MRI, only T1- and T2-mapping, among all single MRI parameters indicating ongoing inflammation and edema, could discriminate between residual inflammation in myocarditis patients and healthy controls at 1–2 months follow-up.[13] In addition, in a small case series implementing parametric imaging on four children with PIMS-TS, elevated T1- and T2-relaxation times paralleled elevated T2 SI ratio in three patients despite lack of visible LGE at 1–4 weeks from diagnosis.[6] Contrary to those findings, in our study, the one case of suspected persistent myocardial edema on T2W images in patient 18 was not supported by elevation of precontrast T1- or T2-relaxation times which have higher diagnostic accuracy. Consequently, this most likely, signifies a false-positive finding.

In a large multicenter analysis on acute cardiovascular manifestations, pericardial effusion, mostly mild to moderate, was reported in 80 (27.9%) patients at admission and reduced to 20.6% during hospitalization.[10] We demonstrated that effusion can be still visible as the only persistent marker of prior PIMS-TS on cardiac MRI in 16% of patients after 3 months. The significance of this finding is unknown and calls for further analyses as the presence of pericardial effusion did not correlate with any markers of the clinical course. Importantly, pericardial effusion was present only in patients with evidence of pericardial effusion during hospitalization and did not appear de novo in any patient during follow-up.

### *Limitations*

Due to pandemic restrictions we were unable to include a control group or to set up our own local reference values for T1- and T2-relaxation times on the new scanner used for the studies. Second, due to limitations of cardiac MRI imaging, we were only able to analyze myocardial complications post PIMS-TS and were not able to detect the frequency and type of coronary artery dilation and aneurysm formation also reported for this disease.[1,2] Finally, despite reassuring results of our study, it is too early to define whether follow-up cardiac MRI should still be recommended at 2–3 months follow-up as suggested by many local protocols of PIMS-TS management.[5]

## Conclusion

There were no persistent changes on cardiac MRI in a group of children studied 3 months post hospitalization due PIMS-TS with cardiac involvement. The comprehensive cardiac MRI assessment in this study supports the hypothesis that cardiac involvement during PIMS-TS is a form of transient inflammatory response rather than direct and potentially persistent injury from the virus.

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